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DRA-2

Dosimetric Verification Given Dose of the prostate as 3D Radiation Therapy based MRI Using Polymer Gel

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Abstract

Polymer gel dosimeter have been developed as means of detecting and verifying an absorbed dose given to cancer patients during radiotherapy in the range of centigrey up to 10 Grey as measured and verifying dose distributions of three-dimensional (3D) treatments. This article reports the dosimetric properties of a new N-isopropanol acrylamide (NIPAM), high weight percent T% ,%C was the mass percent of all co-monomer polymer gel formulation (20T%, 25C%), optimized for magnetic resonance imaging (MRI). In addition, the dosimetric properties include: dose response and sensitivity, energy & LET, temperature effects, gel pH, gel aging and stability, magnetic field strength, dose rate dependence. This study concentrated on assessment of the basic dosimeter properties of a polymer gel evaluated by MRI. The dosimeters were irradiated by 6 and 10MV photons for doses in the range (4–10) Gy. The multi-echo sequence was used for the evaluation of T_2 (spin- spin relaxation time) in the irradiated gel dosimeters. Dependence of $1/T_2$ on the above factors was studied, The purpose of this work was to evaluate the (NIPAM) as monomer N,N'-methylene bis acrylamide a high level dissolved crosslinker where it is a neurotoxin.There is found that no significant dose rate effects in polymer gels were observed using evaluation, although dose response depends on the temperature at which the dosimeter is evaluated. The strength of the magnetic field during evaluation may also influence the dose response. So it is recommended that the gel formulation be imaged between 15–36 h after irradiation.

Keywords: Three-dimensional (3D); Polymer Gel Dosimeter; N-isopropylacrylamide

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1. Introduction

Polymer gel dosimetry is a technique that has the ability to map absorbed radiation dose distributions in three dimensions (3D) with high spatial resolution. Polymer gel dosimeters offer a number of advantages over traditional dosimeters such as ionization chambers, thermoluminescent dosimeters (TLD) and radiographic film. These advantages include independence of radiation direction, radiological soft tissue equivalence, integration of dose for a number of sequential treatment fields, and perhaps most significantly, evaluation of a complete volume at once [1]. The first polymer gel dosimetry system that maintained 3D absorbed dose information –methylene-bis-acrylamide (bis) and acrylamide (AA) co-monomers consisted of N, N infused in an aqueous agarose matrix (Maryanski et al 1992). The purpose of this work was to evaluate the N-isopropyl acrylamide (NIPAM) gel dosimetric characteristics and optimize the protocol for MRI imaging of gel dosimeters for radiation therapy application.

2. Materials and methods

a) Gel preparation

Polymer gels were manufactured using 5 % gelatin, 30 % isopropanol, and 5 mM tetrakis hydroxyl methyl phosphonium chloride (THPC) as antioxidant. The total amount of monomer N-isopropanol acrylamide, and cross linker (N,N' bis acrylamide, Sigma-Aldrich) were varied as needed (6%-20%T) while maintaining equal weights (i.e.50%C) of monomer and cross linker in each gel. The total amount of gel prepared depended on the study (0.25-1L). To begin preapared of isopropanol based normoxic gels, water and iso propanol were heated to 30 ^{o}C at which point gelatin was added. The solution was further heated to 35 ^{o}C at which point the bis cross linker was added. The solution was heated and stirred to 45 ^{o}C, then cooled to 37 ^{o}C and the NIPAM was added. Once all monomers were dissolved, THPC was added. Prepared gel was transferred to 20 mL scintillation vials.[5]

Table.1: Typical 6%T, 50%C Normoxic Poly (NIPAM) Gel Dosimeter

Components/Chemicals	Weight(%)
Desstelated	88%
Acrylamide (AAm)	3.5
N,N-methylene-bis-acrylamide	3.5
Gelatin	5%
total	100%

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Table-2 Chemical composition of the PAG gel dosimeter

Monomer	N-isopropylacylamide (NIPAM)	3g
Crosslinker	N,Ń-methylene-bis acrlamide (Bis)	3g
Gelatin		5g
Water		89
Antioxidant	Tetrakis (hydroxymethl) phosphonium chloride (THPC)	10 mMol

b) Gel irradiation

Gels were irradiated using a Varian Clinac linear accelerator (Varian Inc, Palo Alto, CA, USA) using 6MV photon, a 10 x 10cm^2 field size, and a dose rate of 400 cGy / min at 1.5cm depth in water, for dose response studies, gels were irradiated in a customized phantom for dose ranged from 4 to10Gy. For the imaging application, gels were irradiated in an immobilization device with 3 separate irradiations: (i) a single PDD with 4 Gy at d_{max}, (ii) a two-field cross (~10 Gy at d_{max}), and (iii) a 3-field irradiation. The single and 2-field irradiations were used to generate a calibration curve for the polymer gel dosimeters. This calibration was then applied to the 3-field irradiation in order to convert relative response to dose. All treatment planning was performed for linear accelerator.[8, 11.13]

c) Imaging (MRI Relaxation Time Imaging)

A 0.5 T tesla commercial MRI imaging system (Gyroscan T5 / Philips) was used for imaging purposes. A special wooden mold was constructed to fix in the head coil. The water tank also was stuck to this wooden mold to prevent dislocation of the phantom in the head coil in the scanning processes before and after irradiation. The scanning protocols were also applied before and after irradiation. The data in the MRI console was transferred to the computer (Gyroview) work's station for analysis. For each image an average region of interest (ROI) was obtained and the value of noise was subtracted from this ROI. The data of the signal intensity taken after irradiation was subtracted from than before irradiation to obtain the variation of signal intensity (I) due to irradiation for each region. In this work, two imaging protocols named spin echo (SE) and gradient echo (GRE) were used. In SE technique scanning parameters were as follows: TE=11ms, TR=100, 120, 150, 200, 250, 350, 500, 1000, 2000, 4000ms, slice thickness =10 mm, gap thickness = 0 mm, NSA=2 in GRE technique imaging parameters were as follows: TE=11ms, TR=500 ms, flip angles =30, 60, 75,90 MRI allows the measurement of the longitudinal and transverse relaxation rates (R_1 and R_2) of the dosimeter gels, from which dose maps can be calculated. Conventionally, the corresponding relaxation times are measured, from which the rates can be computed. Relaxation times are

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measured by applying radiofrequency (RF) pulses to excite the magnetization of the spin system, and then sampling during the return to equilibrium. The transverse relaxation time ($T_2 = 1/R_2$) is measured by fitting data collected from at least two points on the transverse relaxation curve following excitation. Knowledge of the RF homogeneity of the RF coils used is useful to assess the effects of sample placement within the coil, which may affect the signal-to-noise ratio in different regions of a gel.Variation in measurements may result from many factors, including changes in RF coil tuning, physical position within the coil, coil loading, imaging slice orientation and room temperature. [2, 7]

d) Evaluation of polymer gel dosimeter

Evaluations of dosimeters were performed on a Siemens Symphony Germany, 0.5T scanner in the head coil one day after irradiation. All samples of the polymer gel dosimeter were left inside the MRI room for a sufficiently long time (2 hours) for temperature equilibrium with the room temperature. A multi echo sequence with 32 equidistant echoes was used for the evaluation of irradiated polymer gel dosimeters. The parameters of the sequence were as follows: TR=3000ms, TE=20ms, slice thickness 4=mm and field of vavorite (FOV) =256mm. [7, 12]

e) Calibration of the dosimeter

The accuracy and sensitivity of an individual gel batch is dependent upon the exact conditions of prepration and the purity of chemicals used. It is therefore recommended that each gel batch is calibrated separately at the time of use. Several different methods of dosimeter calibration have been reported. In all cases, a quantity of the gel batch to be used experimentally is transferred to a calibration phantom and irradiated with a range of known doses. MRI of the calibration phantom produces a $1/T_2$ relaxation map and a plot of known dose against relaxation rate $R_2 = (I / T_2)$ was carried out.

Nine borosilicate glass vials were used to obtain calibration curves. Vial 1 is designated as the unirradiated vial. Vials 2-4 are irradiated with 4MV photons for total doses of 1, 4 and 7Gy, respectively, at a dose rate of 250 MU/min. Vials 5-9 are irradiated with 10MV photons. Vials 5 and 6 are irradiated to a total dose of 1 Gy with a dose rate of 400 and 500 MU/min, respectively; Vials 7-9 receive total doses of 4, 7 and 9Gy, respectively at dose rate of 400MU/min.The cylindrical vials are placed in a cubic water-filled phantom (35cm x 35cm x 38cm) where a photon beam from the Varian Clinac 21EX is administered parallel to the cylindrical axis. The vials are positioned vertically at the bottom of the water tank with approximately 10cm of water above the vials. A gantry angle of 0° and a field size of 10 x 10 cm^2 is used to irradiate the tank. The Varian Clinac 21EX is calibrated to give a dose of 1cGy/MU at d_{max} (SSD=100cm, FS = 10x10cm^2), where is at a depth of 1.2 cm for 4 MeV and 2.5 cm for d_{max} 10MV. The radiation beam passes through 1 cm acrylic and 1mm glass at the bottom of the tube. Because the MRI slices are 2mm thick, it is expected that the slice

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containing the maximum dose is slice 1 for the 4MV photons and slice7 or 8 for the 10MV photons. Because of the potential for vial misalignment, the slice at which dmax occurs is not precise. For the background vial, transverse relaxation rates (R_2) are computed for slices 6, 7 and 8 for the 10MV photons and slices 1,2 and 3 for the 4MV photons.The smallest value observed in these R_2 slices is designated as the value for vial 1. For the irradiated vials, one axial slice in each vial receives the desired dose R_2 at dmax. Within these vials, is computed for the first axial slices 6, 7 and 8 for the 10MV beam and slices 1,2 and 3 for the 4MV beam. The largest value is used as the R_2. A graph of verses absorbed dose is produced, which is the calibration curve. Two calibration curves are computed, one that includes background subtraction (y-intercept=0) and one that does not include background subtraction (non-zero intercept). The slope of the linear portion of the calibration curve gives the gel sensitivity. The storage, irradiation and temperature during MR imaging of the gel vials used for dose calibration and the large experimental gel were kept under identical conditions. All MRI scanning is performed at the same time post-irradiation. [4,6]

3. Results and Discussion

The polymerization reaction is found to be stabilize at 15h post-irradiation. Spatial stability investigations reveal a small overshoot in response for gels imaged later than 36h post-irradiation. Based on these findings, it is recommended that the modified gel formulation could be imaged between (15–36) hours after irradiation. Intra- and inter-batch reproducibility is found to be excellent over the entire range of doses studied in the range (0–20Gy).A significant dose rate dependence is found for gels irradiated between (100–600) MU/min. 4MV-R_2 Dose calibration curve obtained from the calibration vials. Units for dose are in Gy and units for relaxation rate (R_2) are inverse seconds (1/S). Three vials were irradiated to 1.02Gy, 4.08Gy and 7.14Gy, while one vial was left unirradiated for a background measurement. Also shown is the linear fit to the line and R_2 value. The R_2 -dose calibration curves for the 4 and 10MV irradiation beams are shown in Figures1and 2, respectively. The 10MV calibration curves were used to obtain dose rate (R_2) maps from the polymer gel. Such graphs show the slope, y-intercept and chi-squared (R^2) values for both beams. The graphs are linear up to 7.14Gy ($R^2 = 0.989$) for the 4MV photons and 9.18Gy ($R^2 = 0.994$) for 10MV photons. The y-intercept values were nearly in both graphs with an intercept of 4.497 for 4MV photons and 4.695 for the 10MV.

3.1 Dose Volume Histograms

The dose volume histogram (DVH) is a tool employed to assess the radiation dose targeting a specific volume calculated by planning system. DVHs are measured using the treatment planning system by combining all the dose information for a shaped structure.
Figure.3 shows a DVH for a prostate treatment. On this DVH the volumes shown are the rectum, bladder, right femur, left femur and the planning treatment volume (PTV). The dose

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received by the femurs is reasonably low (less than 5% of the volume receiving 50% of the total dose) in comparison with the dose to the PTV (60% of the volume receiving 100% of the dose). An ideal plan would have 100% of the PTV receiving 100% of the dose, while all of the significant structures would receive 0% of the dose.

3.2 Dose response and sensitivity

Figure.3 represents the dose response in gel dosimetry in terms of R_2 relaxation rate versus absorbed dose. The R_2 dose sensitivity, calculated from the initial gradient of the quasi-linear part of an R_2 versus absorbed dose graph, is often quoted as the parameter defining the performance of the gel dosimeter. There has been a general assumption by numerous groups working in the polymer gel dosimetry field of the existence of a linear relationship between R_2 and absorbed dose. However, as previously stated, it has been observed that the relationship is only quasi-linear. A number of studies have shown that altering both the percentage and chemical composition of the constituent chemicals of polymer gel dosimeters will alter the response to radiation. [2,3,7] The R_2 dose sensitivity has been shows an increase in the percentage of co monomers, up to a maximum value above which the monomer will not dissolve. A number of studies have utilized alternative monomers.[14]

3.3 Energy and LET dependence

Depending on the photon energy (E) of x-ray and γ radiation, different interaction processes between the photons and the absorbing medium may occur: photoelectric absorption (E < 500keV), Compton scattering (100keV< E <10MeV) and pair production (E > 1.02MeV). Nevertheless, for radiation such as x and γ rays with low LET, shows that there is no photon energy dependence of a gel dosimeter for photon beam qualities between 6MV and 20MV.

3.4 Temperature

The temperature of the gel at irradiation is reported to have little effect on final R_2 measurements. However, at imaging the sensitivity of the gel increases with decreasing temperature Figure 6 shows that the dose response of a gel imaged at different temperatures between 5°C and 25°C, as demonstrated Polymer Gel Dosimetry for Radiation Therapy.

Figure.6 represents also the effect of temperature during imaging on the water R2 spin-spin relaxation rate dose response curve. The effect is explained by the change in proton correlation times and proton exchange rates in the gel with temperature. These increase as the motions of the polymer chains become slower with decreasing temperature. The relaxation rate of gelatin increases with decreasing temperature. It is therefore important that a gel is allowed to equilibrate to a uniform temperature prior to MRI and that the experimental gel and the calibration gels be at the same temperature.

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3.5 Gel pH

For gelatin, R2 increases with pH at all temperatures and concentrations Maryanski et al (14) noted that a more reproducible dose-response was achieved with neutral gel pH following initial studies with acidic gels. In simple gels constructed only from solutions of Acrylamide, bis Acrylamide, and polymerized by chemical means, an increase in pH (greater than PH 7-8) was also associated with an increase in relaxation rate. This is consistent with a chemical-exchange mediated interaction between water protons and the polymer. Other study indicated that the dependence of relaxation rate on pH was not entirely consistent with a simple acid / base catalyzed chemical exchange.

3.6 Gel ageing & stability

It is not clear whether the saturation doses employed in MRI studies lead to complete polymerization. It may take from a few hours to perhaps several weeks for the polymerization reactions to be complete after irradiation, with the reaction slowing down Quasi-exponentially. Imaging within few hours of irradiation (when the rate of polymerization is greatest) could lead to errors, particularly if there is a time delay between imaging a set of calibration gels and the target phantom.

3.7 Magnetic field strength

The dose response of polymer gel dosimeters has been shown to have some dependence on the field strength of the MRI system with which the dosimeters are evaluated.

3.8 Dependency of Dose Rates

R_2 values were obtained by delivering 2 Gy and 6 Gy at dose rates of 200 MU/min and 400 MU/min to the modified polymer gel. The reproducibility in the investigation of the dose rate dependency was less than 3% in all cases. The absorbed doses were produced by substituting the measured R_2 values to the calibration curves obtained in the examination of the dose reproducibility and accuracy. As a result, the dose accuracy that represents the difference from the absorbed dose obtained by using an ionization chamber showed excellent results, such as 1.63%, [2, 3, and 7].

4. Conclusions

Polymer gel dosimeter offers a method of acquiring 3D maps of complex radiotherapy dose distributions with a spatial resolution of the order of 1mm, depending upon the scanning and imaging specifications. Careful control of a number of factors in the manufacturing process is important so that a gel of good quality can be produced, represents the dose response in gel dosimeter has been represented in terms of an R2 relaxation rate versus absorbed dose, shows that no photon energy dependence of a gel dosimeter for photon beam qualities between 4MV

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and 20MV, there is a little effect on final R2 measurements. However, at imaging the sensitivity of the gel increases with decreasing temperature, the saturation doses employed in NMR studies lead to complete polymerization show that the stability quasi-exponentially with the reaction slowing down. However, much work remains to be undertaken to characterize the modified polymer gel.

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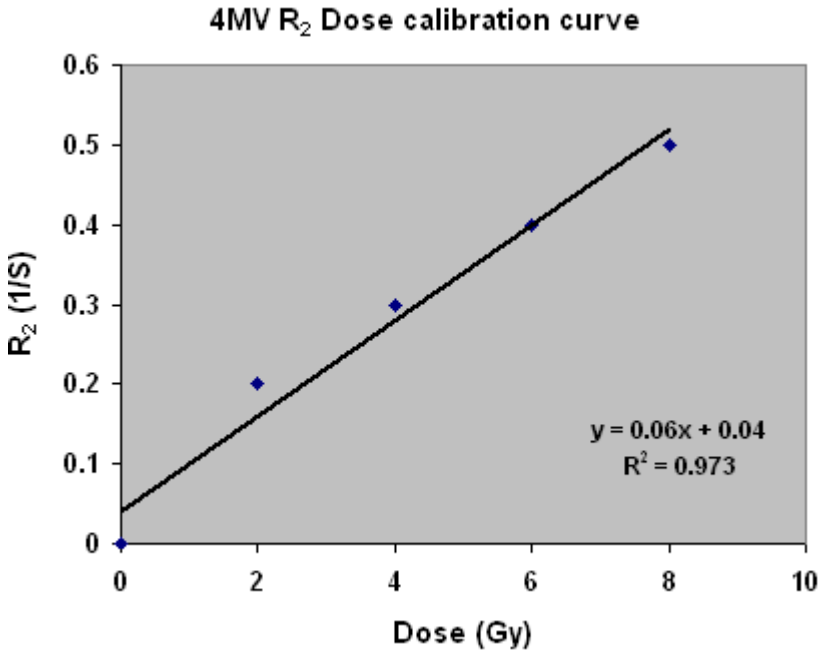

Figure.1: R_2 Dose calibration curve obtained from the calibration vials.

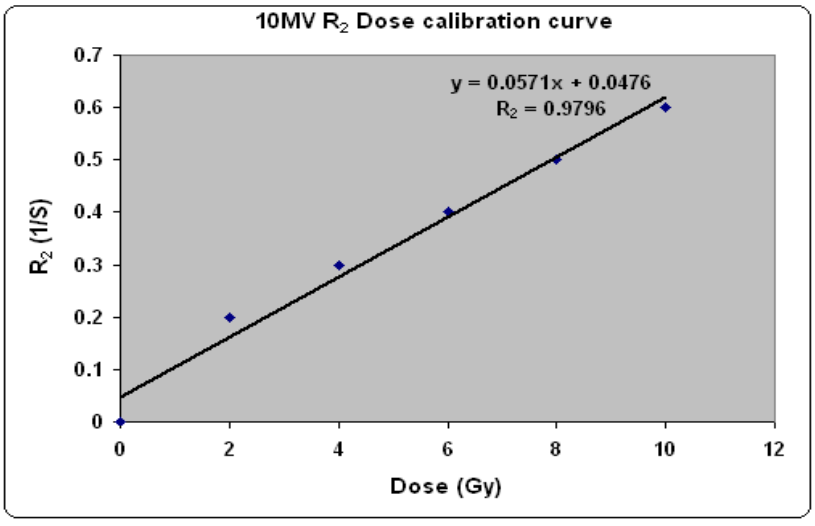

Figure. 2: 10MV- R_2 Dose calibration curve obtained from the calibration vials.

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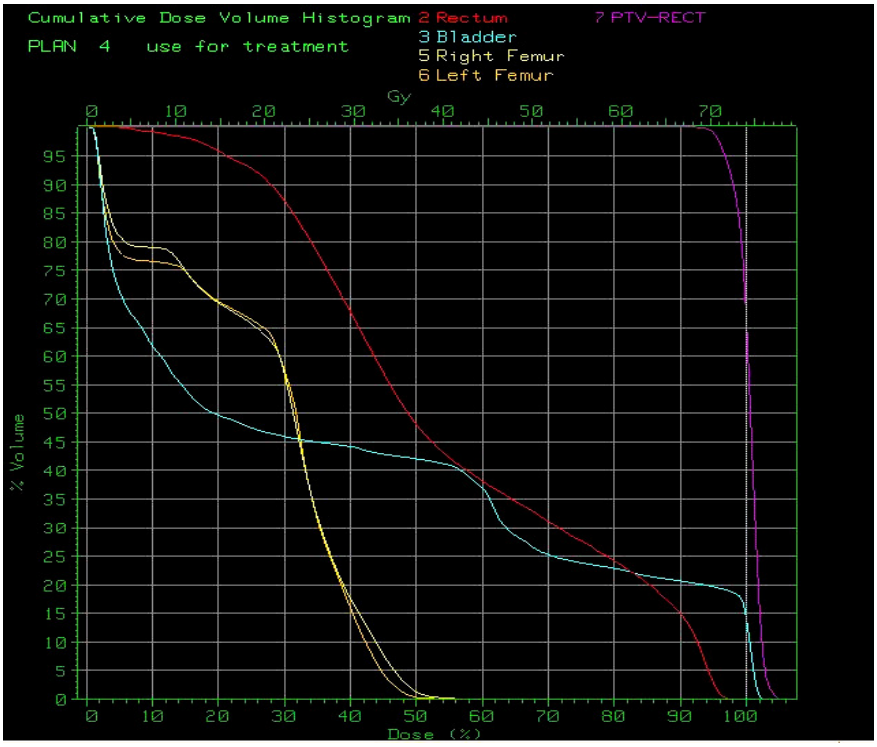

Figure.3 Dose volume histogram for a prostate treatmen

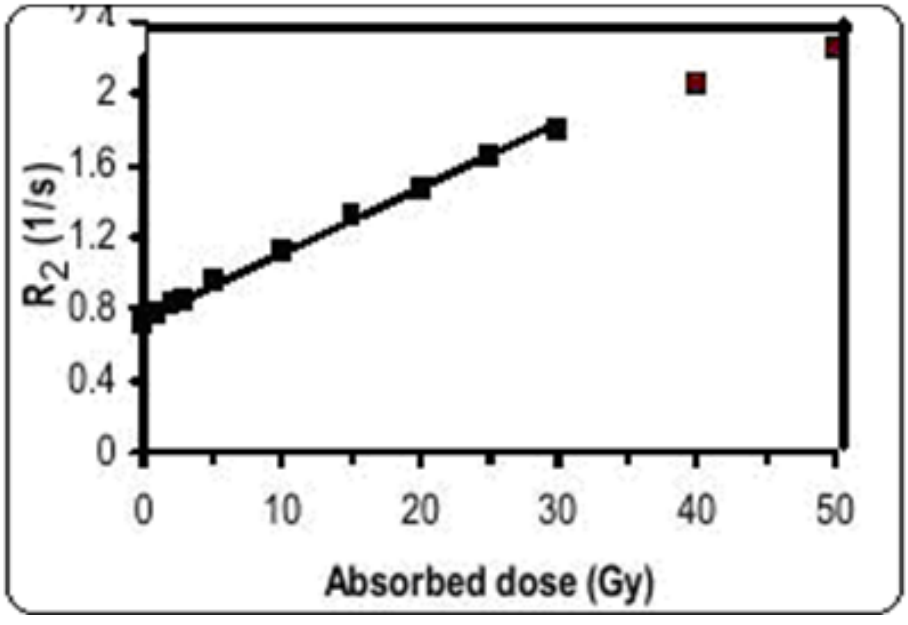

Figure .4: R_2 as a function of absorbed dose one day post irradiation

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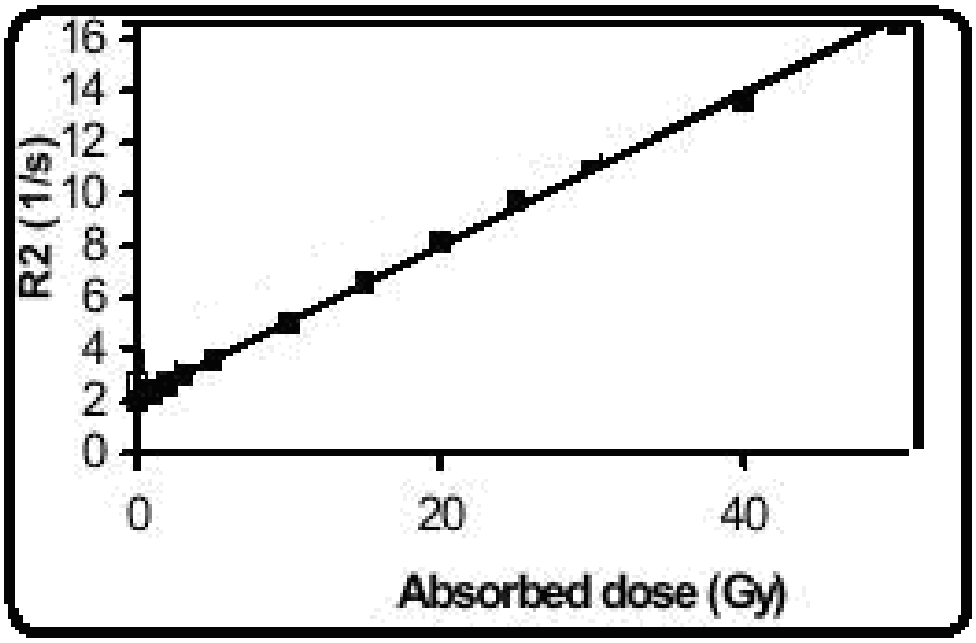

Figure .5: R_2 as a function of absorbed dose three weeks post irradiation.

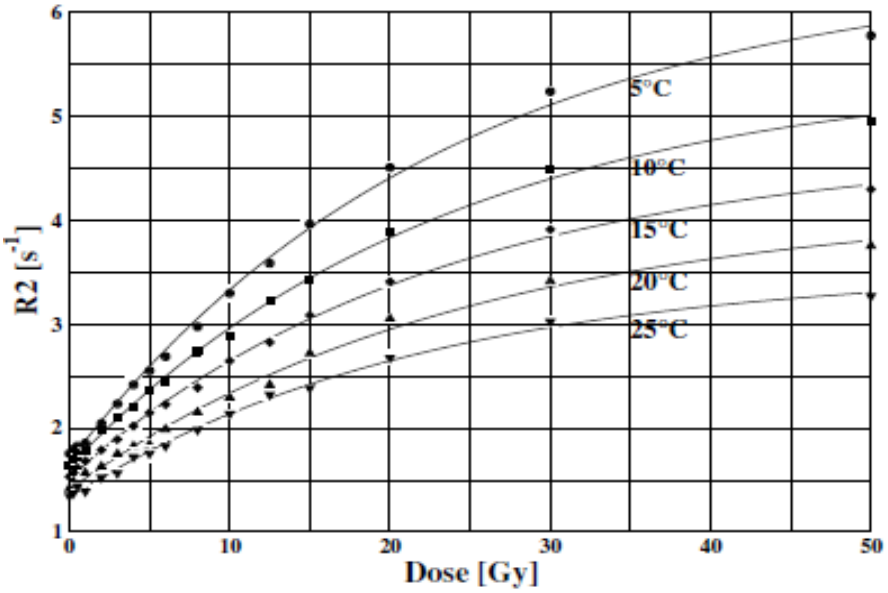

Figure. 6: Temperature dependence of calibration curve.

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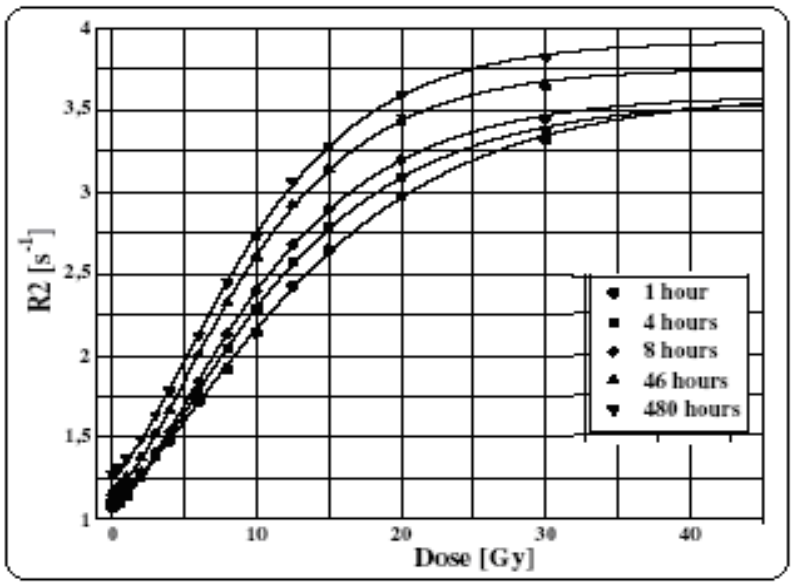

Figure .7: The MRI-measured dose response of a NIPAM at different times after Irradiation

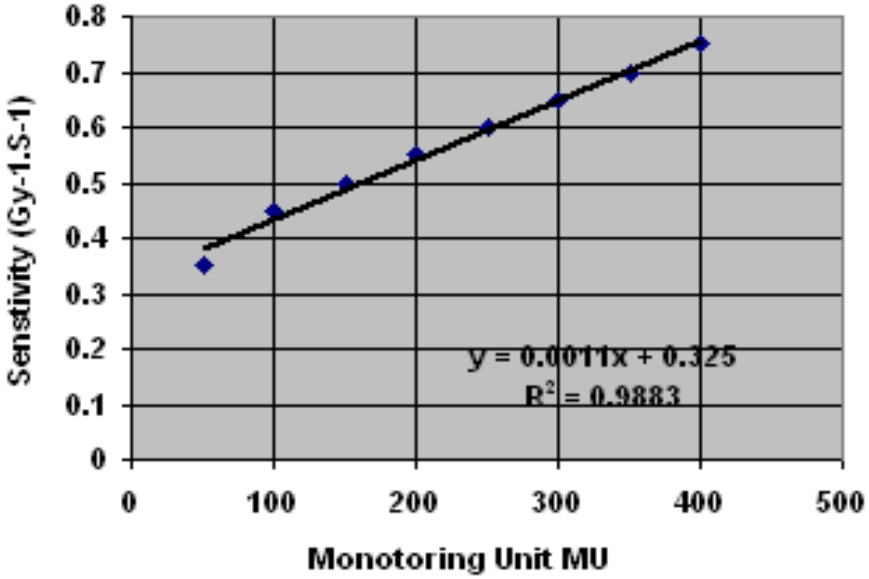

Figure. 8: Dose rate dependence of dosimeter